Effect of community-based voluntary counselling and testing on HIV incidence and social and behavioural outcomes (NIMH Project Accept; HPTN 043): a cluster-randomised trial

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Summary

Background Although several interventions have shown reduced HIV incidence in clinical trials, the community-level effect of effective interventions on the epidemic when scaled up is unknown. We investigated whether a multicomponent, multilevel social and behavioural prevention strategy could reduce HIV incidence, increase HIV testing, reduce HIV risk behaviour, and change social and behavioural norms.

Methods For this phase 3 cluster-randomised controlled trial, 34 communities in four sites in Africa and 14 communities in Thailand were randomly allocated in matched pairs to receive 36 months of community-based voluntary counselling and testing for HIV (intervention group) or standard counselling and testing alone (control group) between January, 2001, and December, 2011. The intervention was designed to make testing more accessible in communities, engage communities through outreach, and provide support services after testing. Randomisation was done by a computer-generated code and was not masked. Data were collected at baseline (n=14 567) and after intervention (n=56 683) by cross-sectional random surveys of community residents aged 18–32 years. The primary outcome was HIV incidence and was estimated with a cross-sectional multi-assay algorithm and antiretroviral drug screening assay. Thailand was excluded from incidence analyses because of low HIV prevalence. This trial is registered at ClinicalTrials.gov, number NCT00203749.

Findings The estimated incidence of HIV in the intervention group was 1·52% versus 1·81% in the control group with an estimated reduction in HIV incidence of 13·9% (relative risk [RR] 0·86, 95% CI 0·73–1·02; p=0·082). HIV incidence was significantly reduced in women older than 24 years (RR=0·70, 0·54–0·90; p=0·0085), but not in other age or sex subgroups. Community-based voluntary counselling and testing increased testing rates by 25% overall (12–39; p=0·0003), by 45% (25–69; p<0·0001) in men and 15% (3–28; p=0·013) in women. No overall effect on sexual risk behaviour was recorded. Social norms regarding HIV testing were improved by 6% (95% CI 3–9) in communities in the intervention group.

Interpretation These results are sufficiently robust, especially when taking into consideration the combined results of modest reductions in HIV incidence combined with increases in HIV testing and reductions in HIV risk behaviour, to recommend the Project Accept approach as an integral part of all interventions (including treatment as prevention) to reduce HIV transmission at the community level.

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Introduction

Several interventions have led to reduced HIV incidence in clinical trials, including early treatment of HIV infection,[1,2] use of antiretroviral therapy to prevent mother-to-child transmission,[3,4] chemoprophylaxis,[5,6] and male circumcision.[7–9] The challenge is to show community-level effects on the epidemic when effective interventions are scaled up.[10]

NIMH Project Accept (HPTN 043) was the first cluster-randomised trial to test whether a theory-based, multicomponent, multilevel social and behavioural prevention strategy could reduce HIV incidence within entire communities. The study hypothesis was that community-based voluntary counselling and testing for HIV compared with standard voluntary counselling and testing would improve community norms about testing, reduce risk behaviours, reduce stigma about HIV, promptly link individuals with HIV to available services, and decrease disease incidence. A major goal of the intervention was to reduce logistical barriers to HIV testing. The intervention was designed to adapt dynamically to changes arising in the communities with real-time performance feedback.

We have previously reported the baseline characteristics of the study population[11] and methods and uptake of the

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intervention.[12] At three trial sites, more HIV tests were done and more HIV infections were newly detected in communities with community-based voluntary counselling and testing than in communities with the standard intervention.

We report findings of the analysis of HIV incidence, the primary outcome of Project Accept, and those of secondary social and behavioural outcomes. All outcomes were assessed at the community level, irrespective of participation in the intervention.

Methods

Study design and participants

Project Accept was a cluster-randomised trial done in 34 communities at four sites in Africa (Soweto and KwaZulu-Natal, South Africa; Tanzania; and Zimbabwe) and in 14 communities in Thailand between January, 2001, and December, 2011. Baseline demographic, behavioural, and social data were collected from a random sample of community residents aged between 18 and 32 years,[11] followed by community randomisation and a 36-month intervention.[13] Eligibility criteria for participation in the baseline assessment and post-intervention assessment were: age 18–32 years, present residency in the community, and ability to provide informed consent. Participation in all intervention activities and services was open to all individuals aged 16 years and older. The effect of the study intervention was assessed across entire communities in one cross-sectional survey done at the end of the intervention. The study protocol, operation manuals, and standard operating procedures are publicly available.[14] Figure 1 shows a timeline for the study.

The trial was done in close partnership with established community advisory boards and local government departments. Oral consent was obtained at the community level for trial participation and randomisation. Participation in all intervention activities was voluntary. To approach household members to participate in the post-intervention assessment, investigators needed permission from the head of the household. Oral consent was obtained from each participant for each component of data collection and for collection and testing of blood samples. The study was approved by ethics committees for each site and by all participating academic institutions.

Randomisation and masking

The communities in each site were located in geographical areas with defined boundaries.[11] At the African sites, the communities were close, but in most cases were not immediately adjacent to each other. The population size of communities varied from 5000 to 15 000 at four sites; at the Soweto site, the typical population size was between 15 000 and 25 000.

The communities were matched into pairs before randomisation on the basis of sociodemographic, cultural, and infrastructure characteristics established by formative research.[15,16] Within each pair, one community was randomly assigned to receive community-based voluntary counselling and testing, the other received standard voluntary counselling and testing alone. Randomisation was done centrally by a sequence of random numbers generated by the Mersenne-Twister random number generator implemented in R. The seed was derived from the system time recorded at the moment the randomisation was done. The randomisation code was written and run by the protocol statistician at the Statistical Centre at Charles University in Prague, Czech Republic.[17] Because of the nature of the intervention, the assignment was not masked, except at the laboratories that analysed study samples (the laboratory staff were unaware of intervention assignment of individual communities).

Procedures

The community-based voluntary counselling and testing intervention was designed to change the context in which individuals and communities respond to HIV with four main components.[13] The community mobilisation component used outreach coordinators and early testers as outreach workers to modify norms for HIV testing,

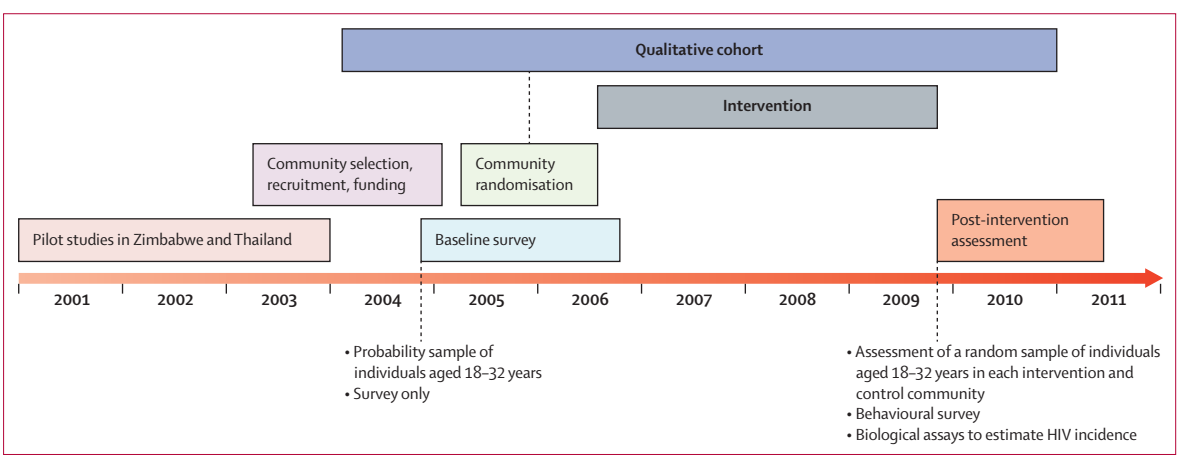

Figure 1: **Study timeline**

encourage discussion about HIV testing and disclosure of HIV status, increase uptake of testing, and reduce stigma. The easy access to voluntary counselling and testing component was designed to increase awareness of HIV status through easily accessible voluntary counselling and testing services provided in mobile units. The post-test support services component provided peer-based social support groups for those who had been tested, irrespective of test results. Topics included, for example, social benefits and harms, status disclosure, access to HIV-related services, advances in HIV treatment, and risk of HIV transmission. The real-time performance feedback component ensured that pre-set intervention goals were met (appendix p 1).[13] Standard voluntary counselling and testing consisted of services at existing district hospitals or local health-care facilities, which were also available in communities with the community-based intervention. The intervention and its adaptation to various settings have been described elsewhere.[13,18–20]

Data were collected in random samples of community residents, irrespective of their participation in intervention activities. The baseline assessment was done before randomisation and did not include HIV testing.[11] The post-intervention assessment was independent of the baseline assessment. Households were selected with equal probability from a complete listing of community households. At baseline, one eligible individual was randomly selected from each household to provide detailed demographic and behavioural data. At the post-intervention assessment, all eligible individuals from the selected households were invited to participate in a brief survey and collection of blood samples. In a random subsample of all the households, one eligible participant was randomly selected to complete a detailed demographic and behavioural questionnaire (appendix p 2).

Study implementation was supervised and managed by principal investigators and project managers at the study sites. A steering committee of 11 members had a conference call every month, and met in person twice a year to design and approve all study procedures, monitor study progress, and approve all modifications and study publications. The NIMH constituted a Data and Safety Monitoring Board and Study Monitoring Committee that convened twice a year to ensure that all study objectives were being met and that the safety of study participants was not compromised. Real-time performance feedback was provided every month to each study team to ensure that study objectives were being met.

Outcomes

The primary outcome of Project Accept was HIV incidence. Secondary outcomes were social and behavioural: sexual risk behaviour, HIV testing rates, social norms regarding testing, discussions about HIV, disclosure of HIV status, stigma associated with HIV, and HIV-related negative life events.

HIV incidence was assessed by analysis of cross-sectional samples collected during the post-intervention assessment. Samples were tested in-country with HIV rapid tests; details of testing are reported by Laeyendecker and colleagues.[21] The final HIV status of study participants was established at the HPTN Network Laboratory at Johns Hopkins University (MD, USA).[21] HIV incidence was assessed with a multi-assay algorithm that included the BED capture immunoassay, an antibody avidity assay, CD4 cell count (obtained at study sites), and HIV viral load (obtained at the HPTN Network Laboratory for a subset of samples).[21] The algorithm was developed and validated with data obtained for 4166 samples from 2882 individuals with known duration of infection (from 1 month to >10 years) from seven African cohorts.[22] It was optimised to detect a difference in HIV incidence between southern African populations. An antiretroviral drug screening assay was used to exclude individuals on antiretroviral therapy from the incidence assessment.[21] Early and acute infections were identified with testing algorithms that included serological and HIV RNA assays.[21]

See Online for appendix

Behavioural outcome measures were assessed with questionnaires administered by interviewers. HIV testing uptake was assessed as the proportion of participants who reported at least one HIV test during the past 12 months. In the post-intervention assessment, testing in the previous 36 months was also assessed. The social norms score was calculated as the mean of scores (ranging from 0 to 3 on a Likert scale) of the participant's responses to six statements assessing their opinion on prevailing community attitudes towards HIV testing (a higher value is associated with more positive attitudes). HIV behaviour risk score was assessed with self-reports of monthly number of unprotected sexual acts averaged during the past 6 months. Number of sexual partners was also recorded in subanalyses. Individuals who were not sexually active in the past 6 months were assigned a score of zero. Negative life events were assessed as the proportion of participants who reported any events related to partnership break-up, discrimination, estrangement, neglect, or violence. Discussions about HIV were measured by the proportion of participants who reported having any HIV-related conversation in the past 6 months. Disclosure of HIV status was measured as the proportion of tested participants who disclosed their HIV test results to another person. HIV stigma score was calculated as the mean of scores (on a 0 to 4 point Likert scale) assigned to validated 28 stigma-related scale items.[23,24] A higher score was associated with more stigma.

Protocol changes

During the study, several unexpected events warranted changes in the protocol. First, one community pair in Soweto was removed from the study soon after the start of the intervention because of threats of political violence. This community pair was replaced by another; a separate

randomisation was done for the new pair and all study activities were undertaken as outlined. Data from the withdrawn community pair were not included in any analyses. Second, the original study plan was to establish the primary HIV incidence outcome with BED capture immunoassay alone. The laboratory plan was revised because of serious concerns about the validity of this approach.[25] Third, the HIV prevalence in the 14 Thai communities was very low (about 1%). Therefore, the incidence assessment was restricted to the 34 African communities. Fourth, findings of quality assurance testing showed that some stored samples from the Soweto site were cross-contaminated,[21] and could not be assessed at the HPTN Network Laboratory.

Statistical analysis

The sample size (seven pairs in Thailand with 500 assessment participants per community; five pairs in Tanzania with 900 assessment participants per community; four pairs at the other sites with 1430 assessment participants per community) was calculated by an adaptation of methods suggested by Hayes and Bennett[26] to provide 80% power to detect a 35% reduction in HIV incidence. The assumptions behind the sample size calculation were 30% prevalence, 3% annual incidence, follow-up duration of 6 months, no misclassification of incident infections, and coefficient of variation 0·26. The power was recalculated after HIV prevalence in the communities was established, and the testing algorithm used for the HIV incidence assessment was developed and validated. With a weighted *t* test, the study provided more than 90% power to detect a 35% reduction in HIV incidence.

The intervention effect for each community pair was calculated as a log incidence ratio for the intervention versus the control group. The overall intervention effect was estimated by the weighted mean of pair-specific effects; the weights were proportional to the harmonic mean of the number of incident infections recorded in the paired communities. The weighted paired *t* test was used to test the hypothesis of no intervention effect at the two-sided level of 5%. CIs were based on the weighted paired *t* statistic. The number of degrees of freedom of the reference *t* distribution was adjusted to take into account unequal weights (the primary analysis used 9·4 degrees of freedom in 17 pairs). The approximate degrees of freedom were calculated as the inverse of the sum of squared weights minus 1 (if the weights were all equal, this yielded a degree of freedom of 16 for the classic *t* test; the test is asymptotic). We verified via simulations that the *t* distribution with approximated degrees of freedom provided better results in small samples (correct level and correct CI coverage) than did the *t* distribution used with the classic *t* test or the limiting standard normal distribution. Subgroup analyses by age and sex were done with the same methods on a subset of the data; these analyses were prespecified in the protocol.

For each behavioural outcome, community-specific means were calculated at baseline (if available) and in the post-intervention assessment. For the outcomes that were measured on one randomly selected household member, the means were weighted by inverse sampling probabilities to adjust for an increased chance of inclusion of participants living in smaller households. Intervention effects were tested with unweighted paired *t* tests on logs of ratios of post-intervention assessment community means to baseline community means. This approach adjusted the intervention effect for baseline differences between the communities. When the baseline mean was not available (36 month testing rates) or baseline data were too sparse (12 month testing rates), the test was done on log post-intervention assessment means only (unadjusted for baseline). Estimates of overall and site-specific means and intervention effects were obtained by exponentiation of averages of community-specific means and intervention effects calculated on the log scale. Two-sided CIs were based on the *t* distribution on the log scale. Subgroup analyses were done by sex, for selected outcomes, and by HIV status, which was established by in-country HIV rapid testing.

This trial is registered at ClinicalTrials.gov, number NCT00203749.

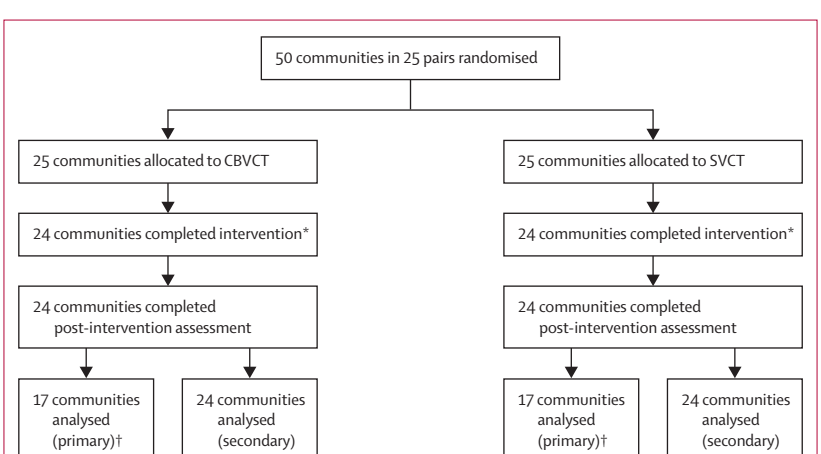

Figure 2: **Trial profile**
CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing. *One community (Soweto) was withdrawn shortly after the initiation of the intervention and replaced. †Seven Thai communities excluded because of low prevalence.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

50 communities were enrolled, matched into pairs, and randomly assigned to the intervention or control group; 48 of the communities received the assigned intervention

and post-intervention assessment (figure 2). Because of low HIV prevalence in the Thai site, only the 34 African communities were included in the primary endpoint analysis (figure 2). All 48 communities participated in secondary outcome analyses.

Table 1 shows the size of the community populations in the post-intervention assessment. Baseline characteristics have been described elsewhere.[11] During the intervention, study teams organised 15 603 community mobilisation activities, provided 71 842 voluntary counselling and testing sessions, and 51 787 support service sessions after testing. The appendix describes the participant flow through the baseline assessment and post-intervention assessment (appendix p 2). Of 84 947 potential housing structures visited during the post-intervention assessment, 9535 (11%) were non-residential (eg, business, storage, or animal structures). 34 828 (41%) households included no eligible participants. The appendix summarises response rates for the primary outcome assessment (appendix). In African sites, nearly 60 000 potentially eligible participants lived in the selected households (appendix p 3). Of them, 8% could not be contacted, 4% refused participation, and 6% were ineligible (appendix). In eligible participants, the response rate for blood sample collection was 94%. When failure to contact participants was taken into account, the

	Thailand		Zimbabwe		Tanzania		KwaZulu-Natal		Soweto	
	CBVCT (N=7)	SVCT (N=7)	CBVCT (N=4)	SVCT (N=4)	CBVCT (N=5)	SVCT (N=5)	CBVCT (N=4)	SVCT (N=4)	CBVCT (N=4)	SVCT (N=4)
Site population (all ages)	55 100	48 100	45 200	48 200	27 500	27 400	33 600	33 600	85 900	66 100
Community population (all ages)	7900 (4900–10 900)	6900 (6300–7600)	11 300 (10 100–12 500)	12 000 (8600–15 800)	5500 (3600–7700)	5500 (3400–6400)	8400 (7000–9400)	8400 (7700–9100)	21 500 (16 600–24 400)	16 500 (5100–23 900)
Site population (age 18–32 years)	9200	6600	10 100	11 000	6000	5700	9800	9500	27 900	20 100
Community population (age 18–32 years)	1300 (800–2100)	900 (800–1200)	2500 (2200–2900)	2700 (1900–3800)	1200 (700–1600)	1100 (700–1300)	2400 (2100–3000)	2400 (2100–2500)	7000 (5300–10 100)	5000 (1500–7300)
Number of households per community (range)	2471 (1626–3276)	2223 (1910–2478)	2888 (2605–3189)	3024 (2233–3712)	1570 (950–1949)	1587 (881–1920)	2588 (2306–2900)	2604 (1801–3134)	4665 (3395–6178)	3642 (1649–5263)
Median household size	3	3	4	4	4	4	4	4	4	4

Data are mean (range) unless otherwise stated. CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing.

Table 1: **Characteristics of the participating communities in the post-intervention assessment**

	Thailand		Zimbabwe		Tanzania		KwaZulu-Natal		Soweto		African sites (total)	
	CBVCT	SVCT	CBVCT	SVCT	CBVCT	SVCT	CBVCT	SVCT	CBVCT	SVCT	CBVCT	SVCT
Initial HIV status (rapid testing)												
Negative	3727 (98%)	3775 (99%)	5126 (87%)	5187 (87%)	4284 (92%)	4028 (92%)	4041 (68%)	4107 (69%)	6116 (87%)	5806 (84%)	19 567 (83%)	19 128 (83%)
Positive	44 (1%)	34 (1%)	788 (13%)	760 (13%)	290 (6%)	252 (6%)	1851 (31%)	1798 (30%)	874 (13%)	1111 (16%)	3803 (16%)	3921 (17%)
Discordant	16 (0%)	23 (1%)	9 (0%)	10 (0%)	110 (2%)	77 (2%)	21 (0%)	25 (0%)	8 (0%)	14 (0%)	148 (1%)	126 (1%)
Final HIV status												
Uninfected	3743 (99%)	3797 (99%)	5146 (87%)	5202 (87%)	4400 (94%)	4105 (94%)	4063 (69%)	4134 (70%)	6134 (88%)	5828 (84%)	19 743 (84%)	19 269 (83%)
Infected*	44 (1%)	35 (1%)	777 (13%)	755 (13%)	284 (6%)	252 (6%)	1850 (31%)	1795 (30%)	712 (10%)	941 (14%)	3623 (15%)	3743 (16%)
Unknown†	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)	152 (2%)	162 (2%)	152 (1%)	163 (1%)
Multi-assay algorithm status (in samples classified as HIV postive)												
Negative	43 (98%)	33 (94%)	750 (97%)	711 (94%)	251 (88%)	228 (91%)	1733 (94%)	1667 (93%)	668 (94%)	879 (93%)	3402 (94%)	3485 (93%)
Positive, acute, and early infections	1 (2%)	2 (6%)	27 (4%)	43 (6%)	33 (12%)	24 (10%)	115 (6%)	127 (7%)	44 (6%)	61 (7%)	219 (6%)	255 (7%)
Not assessed*	0 (0%)	0 (0%)	0 (0%)	1 (0%)	0 (0%)	0 (0%)	2 (0%)	1 (0%)	0 (0%)	1 (0%)	2 (0%)	3 (0%)
Results of antiretroviral drug testing (in samples classified as multi-assay algorithm positive, acute infection, or early infection)												
Antiretroviral drugs detected	0 (0%)	0 (0%)	2 (7%)	1 (2%)	6 (18%)	4 (17%)	5 (4%)	7 (6%)	1 (2%)	3 (5%)	14 (6%)	15 (6%)
No antiretroviral drugs detected‡	1 (100%)	2 (100%)	25 (93%)	42 (98%)	27 (82%)	20 (83%)	110 (96%)	120 (95%)	43 (98%)	58 (95%)	205 (94%)	240 (94%)

CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing. *Five of the 7366 participants who were confirmed as HIV-positive were excluded from the incidence analysis because of missing CD4 cell count data (not assessed by the multi-assay algorithm). †315 participants who had at least one reactive HIV rapid test were excluded from the analysis because it was not possible to confirm their HIV status. This number included 292 participants who were excluded because of sample contamination and 23 participants who were excluded for other reasons.[21] ‡This group includes samples from participants with acute and early HIV infection (those samples were not tested for the presence of antiretroviral drugs) and samples that did not have enough plasma remaining for antiretroviral testing.[21]

Table 2: **Blood sample analysis**

	Thailand		Zimbabwe		Tanzania		KwaZulu-Natal		Soweto		African sites (total)	
	CBVCT (n=3787)	SVCT (n=3832)	CBVCT (n=5923)	SVCT (n=5957)	CBVCT (n=4684)	SVCT (n=4357)	CBVCT (n=5913)	SVCT (n=5929)	CBVCT (n=6846)	SVCT (n=6769)	CBVCT (n=23 366)	SVCT (n=23 012)
Sex												
Men	1947 (51%)	1960 (51%)	2826 (48%)	2924 (49%)	2143 (46%)	2016 (46%)	2483 (42%)	2488 (42%)	3143 (46%)	3159 (47%)	10 595 (45%)	10 587 (46%)
Women	1840 (49%)	1871 (49%)	3094 (52%)	3033 (51%)	2541 (54%)	2340 (54%)	3420 (58%)	3428 (58%)	3698 (54%)	3607 (53%)	12 753 (55%)	12 408 (54%)
Age (men)												
18–24 years	925 (48%)	926 (47%)	1465 (52%)	1530 (52%)	936 (44%)	858 (43%)	1636 (67%)	1665 (68%)	1685 (54%)	1802 (57%)	5722 (54%)	5855 (56%)
25–32 years	1022 (53%)	1033 (53%)	1360 (48%)	1392 (48%)	1205 (56%)	1157 (57%)	815 (33%)	796 (32%)	1454 (46%)	1352 (43%)	4834 (46%)	4697 (44%)
Age (women)												
18–24 years	851 (46%)	853 (46%)	1467 (48%)	1471 (49%)	1129 (44%)	986 (42%)	2006 (59%)	2039 (60%)	1894 (51%)	1951 (54%)	6496 (51%)	6447 (52%)
25–32 years	988 (54%)	1018 (54%)	1624 (53%)	1560 (52%)	1411 (56%)	1353 (58%)	1383 (41%)	1361 (40%)	1803 (49%)	1650 (46%)	6221 (49%)	5924 (48%)
Education												
<5 years	1299 (34%)	794 (21%)	160 (3%)	173 (3%)	1,066 (23%)	1,071 (25%)	121 (2%)	132 (2%)	54 (1%)	60 (1%)	1401 (6%)	1436 (6%)
5–8 years	781 (21%)	787 (21%)	1456 (25%)	1413 (24%)	2788 (60%)	2693 (62%)	388 (7%)	503 (9%)	245 (4%)	241 (4%)	4877 (21%)	4850 (21%)
9–12 years	1423 (38%)	1811 (47%)	3932 (67%)	3976 (67%)	781 (17%)	547 (13%)	5098 (86%)	4971 (84%)	5295 (78%)	5143 (76%)	15 106 (65%)	14 637 (64%)
>12 years	284 (8%)	439 (12%)	366 (6%)	387 (7%)	46 (1%)	41 (1%)	293 (5%)	299 (5%)	1235 (18%)	1305 (19%)	1940 (8%)	2032 (9%)
Marital status												
Single	1045 (28%)	1299 (34%)	1895 (32%)	1849 (31%)	1938 (41%)	1687 (39%)	5730 (98%)	5744 (98%)	6085 (89%)	6200 (92%)	15 648 (67%)	15 480 (68%)
Married	2411 (64%)	2201 (57%)	3381 (57%)	3522 (59%)	2436 (52%)	2378 (55%)	131 (2%)	127 (2%)	677 (10%)	509 (8%)	6625 (28%)	6536 (29%)
Separated	329 (9%)	332 (9%)	641 (11%)	577 (10%)	310 (7%)	287 (7%)	11 (0%)	15 (0%)	54 (1%)	39 (1%)	1016 (4%)	918 (4%)
Sexual activity in the past 6 months												
Active	2770 (83%)	2673 (81%)	4088 (80%)	4208 (80%)	3146 (73%)	3087 (76%)	3767 (74%)	3558 (71%)	5073 (80%)	4963 (80%)	16 074 (77%)	15 816 (77%)

CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing.

Table 3: **Demographic and behavioural characteristics in participants with known final HIV status**

overall response rate was 82%. We recorded no significant difference in the response rate by study group.

The post-intervention assessment included a large proportion of the whole community population (29% of all eligible participants in Soweto and 57–77% of all eligible participants in the other three African sites). Table 2 summarises the results of the blood sample analyses. 46 693 blood samples were collected; 320 (1%) of samples were excluded from incidence assessment (table 2). The HIV incidence analysis included data from 39 012 HIV-negative participants and 7361 HIV-positive participants enrolled at the African sites.[21] 445 samples were classified as potentially incident infections[21] and formed the basis of the HIV incidence analysis (205 in the community group and 240 in the standard testing group); these samples included acute and early infections and multi-assay algorithm positive samples in which antiretroviral drugs were not detected.

Table 3 shows the demographic and behavioural characteristics of the 46 378 study participants with known final HIV status. On average, 54% of these participants were women and a slight majority of men and women were 18–24 years old. On average, the South African sites had more years of education and lower marriage levels than did the other sites in Africa (table 3).

Table 4 shows site-specific HIV prevalence results. The overall HIV prevalence in the African sites was 16·5%. The highest HIV prevalence was recorded in KwaZulu-Natal (table 4); at this site 31% of all participants, more than 50% of participants aged 25–32 years, and more than 60% of women aged 25–32 years were HIV positive (table 4). The other sites had lower HIV prevalence (table 4). At all sites, HIV prevalence in women was more than double that in men, and HIV prevalence in the older age group (25–32 years) was about three times higher than in the younger age group (18–24 years; table 4).

HIV incidence was 1·52% in the intervention groups and 1·81% in the control groups—a borderline significant overall difference of 14% (table 5). The reduction in incidence in women and men was not significant (table 5). Little change in incidence was recorded in the younger age group (RR=0·98); the older age group had a 25% reduction (table 5). The intervention effect was significant in women in the older age group (table 5).

We repeated the analysis with a more stringent multi-assay algorithm, and with a standard paired *t* test rather than a weighted *t* test, and noted very similar intervention effects, but with larger standard errors and wider confidence intervals (data not shown).

Overall, the intervention seemed to reduce incidence at all sites except Tanzania (table 5). The reduction was quite small in KwaZulu-Natal, the site with the highest HIV incidence. In KwaZulu-Natal, the intervention did

not reduce HIV incidence in the younger subgroup or in all women, but in the older subgroup of women incidence was reduced by more than 40%.

The intervention increased HIV testing uptake significantly, and was especially effective in increasing testing in men. Overall 12-month testing rates were 25% higher in the intervention group than in the control group (table 6). The largest effect on testing uptake was recorded in Thailand (56%; appendix p 4). Testing rates during 36 months were 27% higher in the intervention group (table 6). Overall, 49% of the entire 18–32-year-old population living in communities with community-based voluntary counselling and testing was tested during the study, compared with 39% in communities with standard voluntary counselling and testing.

Annual testing rates in men reached 16% after the intervention in the control group, and 24% in the intervention group (table 6), showing a 45% increase over the control group (table 6). At baseline, 12-month testing rates in women were more than twice as large as in men, probably because of antenatal testing. After the interventions were concluded, testing rates in women increased to 34% (control group) and 39% (intervention group), which corresponds to a 15% intervention effect on testing (p=0·0134). Of the individual sites, only Thailand had a meaningful effect on testing in women (appendix p 5). Soweto was the only site that did not show a clear effect on testing rates in men (appendix p 5).

The intervention had a significant effect on community social norms for HIV testing (table 6 and appendix p 6). The mean social norms score was 6% higher in communities with community-based voluntary counselling and testing than in the communities with standard voluntary counselling and testing after adjustment for baseline differences (table 6). The positive change in social norms was greater in men (8% increase) than in women (4% increase), but the intervention effect was significant in both subgroups.

We recorded no effect on sexual risk behaviour measured by the number of unprotected sexual acts (table 6 and appendix p 7). However, in individuals with HIV, a significant reduction of high-risk sexual behaviour was noted in the intervention group. The number of sexual partners of HIV-positive participants was reduced by 8% (95% CI 1–15; p=0·034), and HIV-positive men reduced the number of partners by 18% (95% CI 5–28; p=0·009). Additionally, the proportion of HIV-infected participants reporting multiple partners in the 6 months before interview was 30% lower in the intervention communities than in the control communities (95% CI 8–46; p=0·014). This effect was stronger in men with HIV than in those without; 36% of men with HIV in the control communities reported multiple partners compared with 26% in the intervention communities (29% reduction; 95% CI 11–43; p=0·006). Self-reported multiple partnerships were rare in HIV-positive women.

	Prevalence (%)*		Number of incident samples†		Incidence‡		Effect§	Site weight (%)¶
	CBVCT	SVCT	CBVCT	SVCT	CBVCT	SVCT		
All participants								
Zimbabwe	13·1%	12·7%	25	42	0·68%	1·13%	0·63	13·9%
Tanzania	6·1%	5·8%	27	20	0·86%	0·68%	1·23	10·1%
KwaZulu-Natal	31·3%	30·3%	110	120	3·76%	4·03%	0·93	53·8%
Soweto	12·3%	15·9%	43	58	1·18%	1·63%	0·74	22·2%
Women								
Zimbabwe	17·5%	17·4%	15	27	0·83%	1·51%	0·55	13·2%
Tanzania	8·1%	8·2%	22	16	1·32%	1·05%	1·18	10·9%
KwaZulu-Natal	40·9%	39·0%	77	75	5·26%	4·96%	1·06	53·2%
Soweto	17·3%	22·4%	28	43	1·53%	2·38%	0·67	22·8%
Men								
Zimbabwe	8·3%	7·7%	10	15	0·54%	0·78%	0·99	15·5%
Tanzania	3·6%	3·0%	5	4	||	||	||	4·9%
KwaZulu-Natal	18·0%	18·3%	33	45	2·26%	3·08%	0·73	61·5%
Soweto	6·4%	8·4%	15	15	0·82%	0·84%	0·89	18·1%
Age 18–24 years								
Zimbabwe	5·8%	5·7%	7	19	0·36%	0·94%	0·41	7·8%
Tanzania	2·4%	2·3%	8	4	||	||	||	3·3%
KwaZulu-Natal	18·7%	18·9%	90	79	4·21%	3·65%	1·14	69·4%
Soweto	6·1%	8·2%	20	32	1·08%	1·52%	0·72	19·5%
Age 25–32 years								
Zimbabwe	20·3%	19·7%	18	23	1·06%	1·36%	0·87	21·0%
Tanzania	8·9%	8·3%	19	16	1·12%	0·98%	1·10	19·7%
KwaZulu-Natal	52·7%	50·1%	20	41	2·68%	5·26%	0·51	32·0%
Soweto	19·1%	25·4%	23	25	1·38%	1·79%	0·79	27·3%

CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing. *HIV prevalence of population. †The number of samples from HIV-positive individuals that were classified as multi-assay algorithm positive (excluding samples with antiretroviral drugs detected), and samples from HIV-positive individuals with acute or early infection. ‡Annual rate, calculated across the whole site. §Relative risk of HIV infection (CBVCT *vs* SVCT); weighted average of incidence ratios across community pairs at the site. ¶Percentage contribution of the site to the overall weighted analysis. ||Not enough incident samples to calculate incidence reliably.

Table 4: **Site-specific incidence results for all participants and by sex and age**

The intervention did not affect the proportion of participants who reported having had negative life events or having a conversation about HIV in the past 6 months (table 6). About 80–90% of participants who were tested for HIV reported disclosing their status to at least one person and the proportion did not vary by intervention group (table 6). HIV-related stigma was also not affected by intervention. Baseline mean stigma scores were low, with slight decreases at assessment after intervention (table 6).

Discussion

Findings of Project Accept showed that a multicomponent, multilevel social and behavioural intervention can produce slight reductions in HIV incidence, especially in older women (aged 25–32 years; panel). The intervention did not decrease HIV incidence in young people (aged 18–24 years) or older men. The 30% reduction in HIV incidence in older women was consistent in nearly all community pairs and was highly significant. The intervention improved

HIV testing rates in the peak age range for HIV infection (18–32 years), especially in men; increased the number of people who knew their HIV status; and reduced HIV risk behaviours in people with HIV who might otherwise have transmitted the virus to others. The effectiveness of the intervention was tested in all community residents within the selected age range rather than only in individuals who directly participated in intervention activities.

	Number of incident samples*		Incidence (%)†		Intervention effect‡ (95% CI)	p value§
	CBVCT	SVCT	CBVCT	SVCT		
All participants	205	240	1·52%	1·81%	0·86 (0·73–1·02)	0·082
Analysis by sex						
Women	142	161	2·06%	2·42%	0·88 (0·73–1·06)	0·17
Men	63	79	0·95%	1·19%	0·81 (0·57–1·15)	0·19
Analysis by age						
18–24 years	125	134	1·65%	1·76%	0·98 (0·80–1·22)	0·86
25–32 years	80	105	1·38%	1·90%	0·75 (0·54–1·04)	0·078
Analysis by sex and age						
Women, age 18–24 years	96	96	2·50%	2·55%	1·00 (0·78–1·28)	0·98
Men, age 18–24 years	29	38	0·76%	0·98%	0·95 (0·64–1·40)	0·69
Women, age 25–32 years	46	65	1·54%	2·29%	0·70 (0·54–0·90)	0·0085
Men, age 25–32 years	34	40	1·20%	1·46%	0·78 (0·41–1·47)	0·39

CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing. *The number of samples from HIV-positive individuals that were classified as multi-assay algorithm positive (excluding samples with antiretroviral drugs detected), and samples from HIV-positive individuals with acute or early infection. †Annual rate, calculated across the African sites. ‡Relative risk of HIV infection (CBVCT *vs* SVCT); weighted average of incidence ratios for 17 community pairs. §p value for the hypothesis of no intervention effect on incidence.

Table 5: **Incidence across all African sites**

We do not know why the intervention did not reduce HIV incidence in young people and why most of the effect was concentrated in older women. Possible reasons are the exclusion of Thailand from the analysis, insufficient penetration of the intervention in key HIV-1 transmission groups, and insufficient provision of services (eg, active referral to and maintenance in treatment). The most important behavioural change was reported in HIV-infected men, who reduced the number of sexual partners and occurrence of multiple partnerships. This change could protect the main partners of these men, most likely women older than 25 years. However, a more in-depth analysis is needed to verify this hypothesis. During the trial, antiretroviral therapy (ART) became widely available at most sites. The increased testing rates in intervention communities should have improved treatment coverage and led to reduced incidence. However, the duration of the ART availability during the trial might have been too short to see community-wide reduction in incidence resulting from increased ART uptake. A laboratory assessment is planned to assess ART uptake and to investigate the possible role of treatment in the intervention effect.

This is the first documentation that we could find of a programme that reaches men, increases their HIV testing, and reduces their risk behaviour more than in women. We believe that the increased testing in men compared with women was attributable to more than the higher baseline in women because of more frequent use of the health-care system and thus more routine testing. Increasingly, evidence suggests that men in sub-Saharan Africa are less likely to access testing, and more likely to

	Baseline assessment			Post-intervention assessment			
	Mean outcome in CBVCT communities	Mean outcome in SVCT communities	Ratio*	Mean outcome in CBVCT communities	Mean outcome in SVCT communities	Effect† (95% CI)	p value‡
12-month testing uptake	0·14	0·16	0·87	0·32	0·26	1·25 (1·12–1·39)	0·0003
Men	0·09	0·08	1·13	0·24	0·16	1·45 (1·25–1·69)	<0·0001
Women	0·19	0·22	0·86	0·39	0·34	1·15 (1·03–1·28)	0·013
36-month testing uptake	NA	NA	NA	0·49	0·39	1·27 (1·15–1·41)	<0·0001
Men	NA	NA	NA	0·37	0·25	1·48 (1·29–1·69)	<0·0001
Women	NA	NA	NA	0·59	0·50	1·17 (1·07–1·29)	0·0019
Sexual risk behaviour	3·97	3·76	1·06	4·39	4·27	0·97 (0·89–1·06)	0·53
Social norms regarding testing	1·26	1·25	1·01	1·38	1·29	1·06 (1·03–1·09)	0·0001
Discussions about HIV	0·46	0·46	0·99	0·39	0·39	1·03 (0·92–1·16)	0·56
Disclosure of HIV status	0·81	0·83	0·98	0·87	0·89	0·98 (0·95–1·02)	0·29
HIV-related stigma	1·39	1·37	1·02	1·22	1·21	0·99 (0·96–1·03)	0·74
Negative life events	0·30	0·29	1·01	0·31	0·30	1·02 (0·87–1·20)	0·80

Testing uptake measured by proportion who reported HIV test; sexual risk behaviour measured by self-reported monthly number of unprotected sexual acts; social norms measured by scores ranging from 0 to 3, higher values corresponding to more favourable social norms; discussions about HIV measured by proportion who reported a discussion in the past month; disclosure of HIV status measured by proportion of tested participants who disclosed their last test result; stigma measured by scores ranging from 0 to 4, higher values corresponding to more stigma; negative life events measured by proportion who reported any events related to partnership break-up, discrimination, estrangement, neglect, or violence. CBVCT=community-based voluntary counselling and testing. SVCT=standard voluntary counselling and testing. NA=data not available. *Mean baseline ratio of CBVCT *vs* SVCT communities. †Intervention effect, increase in mean CBVCT:SVCT ratio since baseline (except for testing uptake and disclosure, where the effect is post-intervention assessment CBVCT:SVCT ratio). ‡p value for the hypothesis of no intervention effect on outcome.

Table 6: **Behavioural outcome results**

present for treatment later in their illness and to die sooner from HIV than women. We believe that a Project Accept model that takes testing to the individual rather than having the person come to testing, might be important to test hard-to-reach populations such as men. To reach men in this way might have been important in the reductions in risk behaviour that we recorded in HIV-positive men in the intervention communities.

In Project Accept we showed community-wide effects from an intervention focused on mobilisation, testing, and support. The behavioural results were more significant than was the decrease in HIV incidence. Inclusion of accessible voluntary counselling and testing is likely to be a key component of an integrated combination approach to HIV prevention and care. Additionally, our data suggest that community-wide testing plus treatment programmes can be both safe and feasible. High testing rates are essential for any prevention strategy to be successful. Therefore, Project Accept sets a benchmark for assessment of success of continuing and future combination prevention trials that include a broader range of interventions, including increased provision of treatment for HIV.

This was the first cluster-randomised trial with stigma reduction as a secondary endpoint. However, stigma was low at baseline and had little room to decrease further, possibly because of social desirability bias. Similarly, a recent trial[28] investigating changes in stigma through provision of home-based voluntary counselling and testing in Zambia showed no effect and an overall reduction in stigmatising attitudes from baseline to follow-up. Further work is needed to adequately measure the effect of stigma reduction efforts.

HIV incidence was estimated from a cross-sectional survey done at the end of the intervention period with a multi-assay algorithm developed and validated for this purpose. This was a novel approach in HIV prevention research. We were unable to measure baseline incidence or to use cohort follow-up to estimate incidence because these activities would have interfered with the study intervention. Therefore, we could not adjust for baseline HIV incidence or match the communities on HIV prevalence. Data from our validation studies suggest that the algorithm provided better precision than did 6 months of cohort follow-up.[22] Findings of the validation studies also showed that the multi-assay algorithm had a negligible bias for estimation of the intervention effect, and provided valid tests and confidence intervals. The incidence estimates that we obtained were consistent with those reported in cohort studies done in regions with similar HIV prevalence.[29] Use of ART was addressed by exclusion of infections from the incidence estimate if samples contained antiretroviral drugs.[21]

With the exception of the KwaZulu-Natal site, HIV incidence and prevalence at the African sites was lower than anticipated. Unfortunately the Thailand site had to be excluded because of very low prevalence. Much higher prevalence in Thailand was anticipated because of widespread injection drug use. In some communities, participation rates were lower than desired, which might have affected outcomes. Complete information about the number of tests provided in both the intervention and control communities and the ability to track tests in these communities would have been helpful. In South Africa, no data for testing in the control communities were available and, at all sites, we could not gather data for all testing that took place. We had no control over the various approaches and alternative opportunities for HIV testing that might have been available, and, therefore, we had no alternative but to use self-reported testing data to ensure comparability. However, the self-reports were collected from random probability samples of the community members who might have known that their community was part of a study. The data were collected by assessors who had no knowledge of the participant's serostatus, thus reducing the potential for self-report bias.

Panel: Research in context

Systematic review

A thorough systematic review and meta-analysis of community-based voluntary HIV testing and counselling was published in August, 2013, by Suthar and colleagues.[27] Suthar and colleagues searched PubMed, clinical trial registries, Embase, and WHO Global Index Medicus with no restriction on date or language for studies that included community-based HIV testing and counselling. Search terms are listed in the appendix (appendix p 8). Randomised controlled trials and observational studies were eligible if they included a community-based testing approach and reported one or more of the following outcomes: uptake, proportion receiving their first HIV test, CD4 value at diagnosis, linkage to care, HIV positivity rate, HIV testing and counselling coverage, HIV incidence, or cost per person tested. Suthar and colleagues reviewed 11 community-based strategies for HIV testing and counselling. They used Newcastle-Ottawa Quality Assessment Scale and the Cochrane Collaboration's risk of bias method to assess the risk of bias in studies with a comparator group included in pooled estimates. 117 studies including 864 651 participants completing HIV testing and counselling met the inclusion criteria.

We also did separate searches for every secondary outcome that we studied. We searched PubMed for relevant experimental studies with no restriction on date or language. We searched for studies that used uptake of HIV testing as a primary or secondary outcome, with the following terms: ("HIV testing" OR "VCT") AND ("utilization" OR "uptake") AND ("trial" OR "intervention").

Interpretation

Many studies, including Project Accept, have documented substantial benefit associated with community-based counselling and testing for HIV. However, none have shown decreased HIV incidence and few have documented the effects on special populations at risk (eg, men), HIV risk behaviour, and community social norms regarding HIV. Although many studies have tested the effectiveness of interventions in the uptake of HIV testing, few experimental studies have tested the effect of combined social, behavioural, and structural interventions to address barriers to HIV testing or change in community norms that lead to decreased HIV transmission. Additionally, this study adds to previous scientific literature by assessing the effects of the multi-component intervention at the level of an entire community as opposed to individuals recruited into a clinical trial. The appendix gives a more detailed interpretion of results (appendix p 9).

Results of Project Accept show what is possible when multicomponent mobilisation, testing, and support services are implemented. Even if treatment as prevention is proven effective, the likelihood of implementation in most jurisdictions is low. Our results are sufficiently robust, especially taking the primary and secondary outcomes together, to recommend a combination of mobilisation, mobile testing, post-test support services, and monitoring and assessment of service providers as routine components of public health practice. The results of Project Accept show that slight reductions in HIV incidence can be achieved with a multicomponent, multilevel social and behavioural intervention alone, without scale-up of other services and implementation of structural and biomedical interventions. Project Accept also showed an effective method to increase HIV testing and reduce HIV risk behaviour. High testing rates are essential for any prevention strategy to be successful, and are an essential first step in the implementation of any strategy, especially treatment-as-prevention. Therefore, Project Accept sets a benchmark for assessment of success of continuing and future combination prevention trials that include a broad range of study interventions, including increased provision of ART. The judicious combination and application of behavioural, social, and biomedical interventions should achieve great reductions in HIV incidence in entire communities.

Contributors

TJC, DDC, CEZ, SFM, MS, and GS did the literature search. TJC, MK, DDC, CEZ, SC, AC, GG, JKKM, SFM, LR, MS, HvR, AF, DD, and SHE designed the study. TJC, MK, DDC, CEZ, SC, AC, GG, JKKM, SFM, LR, MS, HvR, NM, AG, OL, EP-M, and SHE collected data. TJC, MK, DDC, CEZ, OL, EP-M, DD, and SHE analysed data. TJC, MK, DDC, CEZ, SC, AC, GG, JKKM, SFM, LR, MS, HvR, NM, AF, OL, EP-M, GS, DD, and SHE interpreted data, wrote the report, and approved the final version of the report.

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Declaration of interests

We declare that we have no competing interests.

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